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Using Microsimulation to Estimate the Future Health and Economic Costs of Salmonellosis under Climate Change in Central Queensland, Australia

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Background: The incidence of salmonellosis, a costly foodborne disease, is rising in Australia. Salmonellosis increases during high temperatures and rainfall, and future incidence is likely to rise under climate change. Allocating funding to preventative strategies would be best informed by accurate estimates of salmonellosis costs under climate change and by knowing which population subgroups will be most affected.

Objective: We used microsimulation models to estimate the health and economic costs of salmonellosis in Central Queensland under climate change between 2016 and 2036 to inform preventative strategies.

Methods: We projected the entire population of Central Queensland to 2036 by simulating births, deaths, and migration, and salmonellosis and two resultant conditions, reactive arthritis and postinfectious irritable bowel syndrome. We estimated salmonellosis risks and costs under baseline conditions and under projected climate conditions for Queensland under the A1FI emissions scenario using composite projections from 6 global climate models (warm with reduced rainfall). We estimated the resulting costs based on direct medical expenditures combined with the value of lost quality-adjusted life years (QALYs) based on willingness-to-pay.

Results: Estimated costs of salmonellosis between 2016 and 2036 increased from 456.0 QALYs (95% CI: 440.3, 473.1) and AUD 29,900,000 million (95% CI: AUD28,900,000, AUD31,600,000), assuming no climate change, to 485.9 QALYs (95% CI: 469.6, 503.5) and AUD31,900,000 (95% CI: AUD30,800,000, AUD33,000,000) under the climate change scenario.

Conclusion: We applied a microsimulation approach to estimate the costs of salmonellosis and its sequelae in Queensland during 2016–2036 under baseline conditions and according to climate change projections. This novel application of microsimulation models demonstrates the models' potential utility to researchers for examining complex interactions between weather and disease to estimate future costs. https://doi.org/10.1289/EHP1370

Introduction

Salmonellosis is a common foodborne bacterial disease in Australia, with >80,000 cases annually [after adjusting for under-reporting; Hall et al. 2008; NNDSS 2016). Salmonellosis presents as gastrointestinal symptoms that last approximately one week. Most patients recover without treatment; however, approximately 9% of patients develop reactive arthritis (ReA), and 10% develop post-infectious irritable bowel syndrome (PI-IBS; Ford et al. 2014; Neal et al. 1997; Thabane et al. 2007). The Australian Department of Health and Ageing estimated that, circa 2004, foodborne diseases, including salmonellosis, cost >AUD1,250,000,000 annually in health care, disease surveillance, and absenteeism (Abelson et al. 2006). These costs were based on the most comprehensive assessment of foodborne disease incidence at the time (Australian epartment of Health and Ageing 2005) and on data obtained primarily from government sources pertaining to the costs of lost productivity for businesses and individuals; health care; premature mortality; food safety recalls; and government foodborne disease surveillance, investigation, and safety systems (Abelson et al. 2006). In addition, reported cases of salmonellosis have increased in Australia from approximately 29 cases per 100,000 people per year in the early 1990s to approximately 60 cases per 100,000 people per year during 2011–2015 (NNDSS 2016). The increasing incidence of salmonellosis in Australia warrants research to inform prevention strategies to reduce the associated costs.

Queensland, the northeastern state of Australia, has a higher salmonellosis incidence than most Australian states. Annual incidence rates have increased from 47 reported cases per 100,000 people in the early 1990s to approximately 83 reported cases per 100,000 people in recent years. Along with improved detection techniques, a possible driver of this increase could be climate change. Several studies have identified associations of warmer temperatures and rainfall patterns with increased salmonellosis incidence across different climatic regions. For example, D'Souza et al. (2004) evaluated monthly salmonellosis cases reported in five Australian cities over a 10-y period and found that the mean temperature in the previous month predicted both monthly salmonellosis notifications and seasonal patterns. A 5°C increase in mean monthly temperature in Brisbane, Queensland's capital city, was associated with a 62% increase in salmonellosis cases (D'Souza et al. 2004). Similarly, Fleury et al. (2006) reported that weekly salmonellosis cases increased with weekly mean temperature in Alberta, Canada, although the same association was not found for the province of Newfoundland and Labrador. In New Zealand, Lal et al. (2013) found that salmonellosis was positively associated with temperature during the current month and with the Southern Oscillation Index (a measure of regional climate conditions related to El Niño) during the current and previous month. Finally, Zhang et al. (2010) reported that a 1°C increase in minimum temperature in the previous fortnight was associated with a 5.8% increase in reported salmonellosis cases in Brisbane, Queensland, and a 1°C increase in the previous month's mean maximum temperature was associated with an 11.9% increase in reported salmonellosis cases in Townsville, Queensland, Australia. Smaller positive associations were also found between rainfall and reported salmonellosis cases in both locations (Zhang et al. 2010).

Warmer temperatures may increase salmonellosis cases because warm days facilitate the growth of *Salmonella* in risky foods, such as eggs and meat, left at room temperature, and altered rainfall patterns can mean that water sources used for

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irrigation of produce or as drinking water may be contaminated (Liu et al. 2013). Therefore, we hypothesized that warmer temperatures and altered rainfall patterns projected for Queensland under climate change might influence the incidence, and the related health and economic costs, of salmonellosis. Estimates of these costs are key to highlighting to policy makers the importance of developing effective preventative strategies to reduce the incidence of salmonellosis.

We have identified only one study to date that has quantified the potential future health costs of salmonellosis in Queensland. The study estimated the morbidity burden of salmonellosis in Brisbane, Queensland's capital city, in 2030 and 2050 under projected climate changes (Zhang et al. 2012). The authors estimated that the warmer projected temperatures, in conjunction with population growth, would result in losses to the population of 80–106 y of health to salmonellosis in 2030 and of 99–129 y in 2050, compared with 53 healthy years lost in 2000, the baseline year (Zhang et al. 2012).

For the present analysis, we estimated the effects and costs of climate change on hospitalizations for severe cases of salmonellosis and on the common sequelae reactive arthritis (ReA) and post-infectious irritable bowel syndrome (PI-IBS), in addition to estimating the effects on the incidence of salmonellosis. In addition, we used microsimulation models to account for dynamic changes in population size and characteristics (age, sex, and salmonellosis risk) over time due to births, migration, death, and the likelihood of moving between health states (e.g., from healthy to contracting salmonellosis, or from salmonellosis to PI-IBS). We used these models to estimate the years of quality life lost because of salmonellosis and its sequelae according to age, sex, and specific disease outcomes, after accounting for changes in incidence as a consequence of climate change, with the goal of informing strategies to reduce the incidence and costs of salmonellosis in the future.

Microsimulation models are an increasingly common method for projecting disease outcomes to inform public health policies, for example, by assessing the cost effectiveness of treatments or the effects of prevention strategies (Rutter et al. 2011). Health-related microsimulations have recently been used to assess the costs of osteoarthritis (Sharif et al. 2015), to model the impact of quality of life on the outcomes of diabetes (Hayes et al. 2011), to project the disability status of older Canadians to inform policies regarding aging populations (Légaré and Décarie 2011), and to estimate the size of the HIV-positive population in the United Kingdom (Nakagawa et al. 2016).

Microsimulation offers advantages over other projection methods such as extrapolation techniques and cohort-component models. Projection by extrapolation takes an incidence rate from a baseline period and applies it to a future population structure to estimate the future incidence of a disease or condition. Extrapolation produces data for discrete time points, typically a baseline year and one or more individual years in the future (Huang et al. 2011). In contrast, microsimulation models incorporate dynamic population fluctuations over the entire simulated period. For example, a microsimulation can account for changes in the size of the at-risk population due to transitions from one health state to another, as well as changes in higher- or lower-risk subpopulations due to demographic shifts, such as shifts in the underlying age structure of a population related to projected changes in birth and death rates.

Our objectives were to estimate the future health and economic costs of salmonellosis in Central Queensland from 2016 to 2036 under baseline and climate change scenarios and to demonstrate that microsimulations are useful models for estimating these costs. We hypothesized that the climate changes projected for Central Queensland by 2036 would increase the costs of salmonellosis. Understanding the potential future costs of salmonellosis under climate change is important for informing the need for and the direction of preventative strategies.

One aim of this study was to show the application of a microsimulation model, including key methodological choices. For a more detailed discussion of methodological details, we recommend Stephen (2017). The R code to implement the model is available on Figshare (https://figshare.com/articles/Annotated_microsimulation_R_code/4876853) and in the Supplemental Materials.

Methods

We developed a microsimulation model to project the Central Queensland population to 2036. The model is graphically represented in Figure 1. Simulated individuals transitioned between healthy and unwell states according to probabilities that we identified from the literature, and the size and characteristics of the simulated population were determined by migration, mortality, and fertility rates based on values obtained from the Australian Bureau of Statistics (see Table 1; ABS 2013a, 2013b, 2015). We ran two versions of the model for the years 2016–2036: a baseline model with no change in climate and a climate change model that accounted for estimated effects of projected changes in temperature and rainfall on the risk of contracting salmonellosis in Central Queensland. We ran 100 simulations of each version, averaged the results of the simulations to account for variation in the populations introduced by the stochastic decisions made within each simulation, and calculated 95% confidence intervals (Rutter et al. 2011). We based our microsimulation models on the MicSim package (version 1.0.12, S. Zinn) in R (version 3.1.2; R Development Core Team), which we adapted to include the health states involved in the salmonellosis disease process, in addition to the existing demographic states such as sex, fertility, and migration.

Microsimulation models have two components: a base population that forms the model's starting point and structured states through which individuals can transition (Figure 1). Several sources of data were required, including *a*) a baseline population, which is a "snapshot" at the start of the simulation of the population to be modeled; *b*) the probability of transitioning between states; *c*) the effects of temperature and rainfall on salmonellosis to model the effect of climate change; *d*) the climate changes projected for Central Queensland; and *e*) population projections to validate the models' simulated population structure.

Study Region

We chose Central Queensland as the study region because it has a large population with a clear association between temperature and rainfall and increased risk of salmonellosis; hence, it is ideal for showing the benefits of microsimulation. Central Queensland is a subtropical region on Australia's east coast (Figure 2) with an estimated population of 243,000 in 2016, as calculated by summing projections for smaller areas comprising Central Queensland (QGSO 2014). Summer temperatures range from 22 to 31°C with an average rainfall of 124 mm, and winter temperatures range from 11 to 23°C with an average rainfall of 28 mm based on data from the Australian Bureau of Meteorology (BOM) for 2004 to 2013 (Climate Data Services team, BOM, written communication, 2014). The average annual incidence of salmonellosis between 2004 and 2013 was approximately 91 cases per 100,000 people, determined from data from the Queensland Health Communicable Disease database (J. Marquess, Queensland Health, personal communication, 2015).

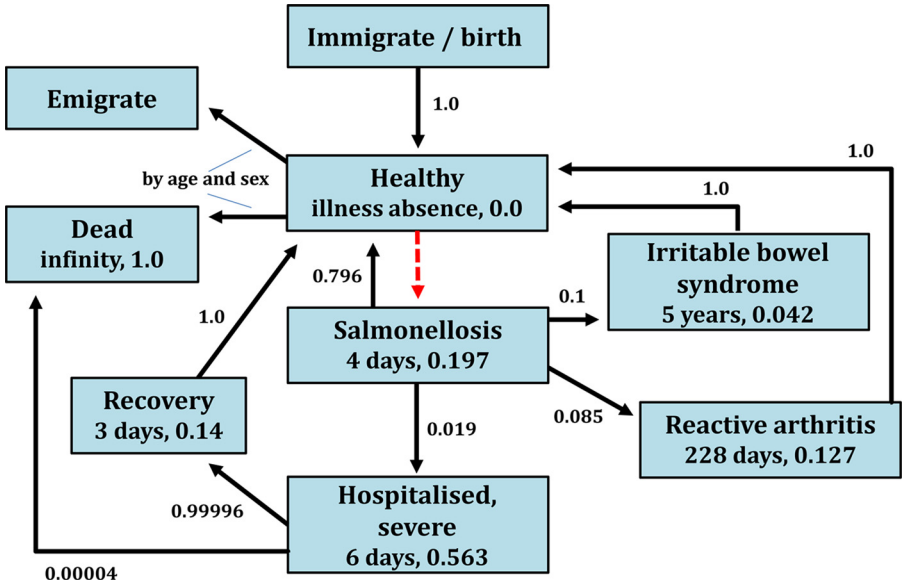

Figure 1. Microsimulation model for salmonellosis. Disability weights [0.0 to 1.0, the proportion of a quality-adjusted life year (QALY) "lost" during each state] and average time spent in the health state are in each state's box, and the overall probability of transitioning between health states is shown along the pathway. Overall probabilities are presented as an example; however, the probabilities in the model varied by age and sex. The dashed arrow represents the difference in the probability of transitioning from "healthy" to "salmonellosis" under the climate change scenario compared with the baseline (no climate change) scenario, that is to say, the influence of the projected change in daily temperatures and rainfall on the incidence of salmonellosis during 2016–2036. The sources of utility weights (from which disability weights were derived by subtracting the utility weight from 1), durations, and transition probabilities are shown in Table 1. The probabilities of dying or emigrating varied substantially by age and sex and therefore have been denoted here as "by age and sex" rather than an overall value.

Base and Projected Populations

The size and structure of the base population corresponded to that of the Central Queensland population on 30 June 2007 (ABS 2008). Each simulated member of the base population was assigned a unique identifier, a birth date (year of birth based on age in 2007, with the specific month and day assigned at random), and sex. In addition, each simulated individual was characterized by number of children (set to 0 for all individuals at the start of the simulation) and initial health status (set as healthy for all individuals at the start of the simulation).

After starting the simulation, the population changed as individuals entered the population through birth and immigration and left through death and emigration. Model parameters for rates of fertility, mortality, and migration were based on estimated age- and sex-specific rates from the ABS. Fertility rates were estimated from the average fertility rate in Central Queensland between 2006 and 2011 (ABS 2013b). Mortality rates (from the healthy state) were based on the risk of death in Queensland in 2012, which was similar to those in adjacent years (ABS 2013a). Immigration rates were estimated by determining the annual number of immigrants entering Central Queensland as the average of the financial years 2006–2007, 2010–2011, and 2013–2014 (ABS 2015). We then multiplied this figure by the number of years being simulated to determine the number of immigrants likely to enter Central Queensland during the simulated period. We estimated the emigration rate as the average number of emigrants from Central Queensland in the financial years 2006–2007, 2010–2011, and 2013–2014 (ABS 2015) divided by the population of Central Queensland in 2011 (QGSO 2014) as a midpoint year for which population data were available. All rates were held constant, but the actual numbers of births, deaths, and migrants varied as the age and sex structure of the population changed over time.

To compare the simulated population with official projections, we obtained age- and sex-specific population projections to 2036 from the Queensland Government Statistician's Office (QGSO) (QGSO 2014) for small areas and aggregated them to correspond to the study region.

Weather Projections

Climate projection data were obtained from the Consistent Climate Scenarios Project (CCSP) operated by the Queensland Department of Science, Information Technology and Innovation (DSITI) (J. Carter, DSITI, written communication, 2016). The CCSP generated daily weather projections in 2030 and 2050 for a 5 km × 5 km grid across Australia using a range of Global Climate Models (GCMs), emissions scenarios, and climate sensitivities.

GCMs are mathematical models of Earth's physical processes, including the atmosphere, oceans, land, and vegetation, which are used to generate long-term climate projections (Burgess et al. 2012). The CCSP generated projections from 19 individual GCMs and composite projections for 4 representative future climate (RFC) groups that included GCMs that differ primarily with regard to rainfall projections and are characterized according to the degree of warming—either warm or hot—in the East Indian and West Pacific Oceans (Burgess et al. 2012; Watterson 2012; see Table S1). For the present analysis, we used composite projections for the West Pacific (WP) RFC group (which included the BCCR, CSIRO-MK30, GFDL-21, IAP-FGOALS-G10, INMCM, and NCAR-CCSM GCMs), which represents a moderate change scenario resulting in a warmer and drier climate in the Queensland area.

In addition, we selected the A1FI emissions scenario to project the effects of future population growth, energy sources, and economic and technological development on climate. The A1FI scenario assumes very rapid economic growth and technological change, population growth that peaks mid-21st century, and continued reliance on fossil fuels (IPCC 2000).

Table 1. Input parameters for microsimulation models.

Input parameter	Value	Source of value	Description of source	Population and time period
Demographic parameters				
Base population	199,539 people disaggregated by age and sex	ABS 2008	National Statistical Organisation data	Central Queensland population as of 30 June 2007
Fertility rate	Rate varied by age (see Stephen 2017)	ABS 2013b	National Statistical Organisation data	All births in Central Queensland between 2006 and 2011
Mortality rate	Rate varied by age and sex (see Stephen 2017)	ABS 2013a	National Statistical Organisation data	All deaths in Central Queensland in 2012
Emigration rate	Rate varied by age and sex (see Stephen 2017)	ABS 2015	National Statistical Organisation data	Average number of emigrants from Central Queensland between 2006 and 2011
Immigration rate	Rate varied by age and sex (see Stephen 2017), total immigrants was 355,371	ABS 2015	National Statistical Organisation data	Average number of immigrants to Central Queensland between 2006 and 2011
Projected population in 2036 for matching purposes	355,409 disaggregated by age and sex	QGSO 2014	State Statistical Organisation data	Projected population based on 2011 population with assumptions about fertility, mortality, and migration.
Weather parameters				
Baseline weather	Daily recordings of minimum and maximum temperature and rainfall in Central Queensland between 2004 and 2013	BOM 2014	National Meteorological Organisation data	No relevant population; data were daily weather recordings for 1 January 2004 to 31 December 2013.
Weather projections	Projected daily rainfall and minimum/maximum temperatures for 2030 and 2050 under the A1FI climate change scenario from the WP group of Global Climate Models based on weather during 1960–2010	DSITI, written communication (2016)	State Government Agency data	No relevant population; data were projected daily minimum/maximum temperature and rainfall for 2030 and 2050.
Incidence parameters				
Adjustment for underreporting of salmonellosis cases	Multiply reported cases by 7	Hall et al. (2008)	Derived from a large observational study and government surveillance	General Australian population between 2000–2005
Adjustment for nonfoodborne salmonellosis cases	Multiply cases adjusted for underreporting by 0.72	Kirk et al. (2014)	Comprehensive review using data predominantly from government agencies	Australian population circa 2010
Adjustment for salmonellosis cases not locally acquired	Multiply cases adjusted for underreporting and transmission type by 0.85	Kirk et al. (2014)	Comprehensive review using data predominantly from government agencies	Australian population circa 2010
Salmonellosis under baseline weather conditions	Rate varied by age and sex	Queensland Health, personal communication, (2015), with adjustments from Hall et al. (2008) and Kirk et al. (2014), and weather data from BOM (2014).	State government communicable disease surveillance database with mandatory reporting, and weather data from the National Meteorological Organisation.	All cases of confirmed salmonellosis in Central Queensland between 2004 and 2013, with adjustments for underreporting, transmission mode and nonlocal acquisition
Salmonellosis under climate change	Rate varied by age, sex and year (see Stephen 2017)	Weather–disease associations calculated in the current study and applied to weather data from DSITI (DSITI, written communication, 2016) .	Calculated as described in "Methods"	All cases of confirmed salmonellosis in Central Queensland between 2004 and 2013, with adjustments for underreporting, transmission mode and nonlocal acquisition
Hospitalization, severe salmonellosis	1.9% of cases	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
Recovery from hospitalization/death from salmonellosis	99.96% of cases 0.04% of cases	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
PI-IBS	10.0% of cases	Thabane et al. (2007)	Comprehensive literature review	Several countries' populations between 1994 and 2006
ReA	8.5% of cases	Ford et al. (2014)	Comprehensive review of case–control, outbreak and cohort studies	Several countries' populations between 1993 and 2005

Table 1. (*Continued.*)

Input parameter	Value	Source of value	Description of source	Population and time period
Utility weights[a]				
Healthy	1		Standard component of Health-Related Quality of Life theory	
Acute salmonellosis	0.803	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
Hospitalization, severe salmonellosis	0.437	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
Recovery from hospitalization	0.860	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
PI-IBS	0.958	Haagsma et al. (2010)	Mild Diseases and Ailments study (MiDAS) with a layperson panel ($n = 105$)	Dutch population circa 2003
ReA	0.873	WHO (2008)	Global Burden of Disease study, update for 2004	Global Burden of Disease study population circa 1990
Dead	0		Standard component of Health-Related Quality of Life theory	
Duration				
Healthy	Whenever not ill		Standard component of Health-Related Quality of Life theory	
Acute salmonellosis	4 days	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
Hospitalization, severe salmonellosis	6 days	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
Recovery from hospitalization	3 days	Batz et al. (2014)	Comprehensive review using expert elicitation, surveillance data and literature review	U.S. population circa 2005
PI-IBS	5 years	Haagsma et al. (2010)	Review of six long-term observational studies	Several populations between 1994 and 2008
ReA	228 days	Minor et al. (2015)	Literature review	U.S. women circa 2002
Dead	Infinite		Standard component of Health-Related Quality of Life theory	
Medical costs[b]				
Acute salmonellosis	AUD42.90 applied to 20% of cases because 80% do not seek medical attention (Hall et al. 2008)	RACGP (2014)	Federal Department of Health medical fee schedule	Australian population circa 2014
Hospitalization	AUD6,872	National Hospital Cost Data Collection (IHPA, 2013)	Federal government agency hospital costings	Australian population circa FY 2012–2013
PI-IBS	AUD1,396, including GP visits, specialist consultations, diagnostic tests and medications based on a 5-y duration of illness.	Costs are from the RACGP (2014), treatment requirements are from Canavan et al. (2014).	Costs are from the federal Department of Health medical fee schedule, medical treatment requirements are from Canavan et al. 2014.	Costs are based on the Australian population circa 2015, treatment requirements are based on a narrative review of 18 studies from several countries

Note: The precise transition probabilities between health states by age, sex, and year under climate change, which correspond to the incidence rates of health conditions, are available in Appendix L of Stephen (2017). ABS, Australian Bureau of Statistics; BOM, Australian Bureau of Meteorology; DSITI, Queensland Department of Science, Information Technology, and Innovation; FY, financial year; GP, general practitioner; PI-IBS, post-infectious irritable bowel syndrome; QGSO, Queensland Government Statistician's Office; RACGP, Royal Australian College of General Practitioners; ReA, reactive arthritis; WHO, World Health Organization; WP, West Pacific.
[a]The weights presented in Figure 1 are disability weights, which correspond with the utility weights presented in Table 1 as 1 − utility weight.
[b]We were unable to identify suitable data to estimate the medical expenditure costs, and as such, the total economic costs, for ReA.

We obtained projections from the WP RFC group for the A1FI scenario from the CCSP for 88 weather stations in Central Queensland for 2030 and 2050. (Although our simulations ended in 2036, we used projections for 2050 to linearly interpolate data for 2031–2036.) Data for each station included the maximum and minimum temperature and rainfall on each day in 2030 and 2050, which were projected from 50 measured baseline values for the same day at each weather station during 1960–2010, resulting in 50 projections for each day in 2030 and 2050. To generate regional climate projections, we calculated a single set of daily projections for 2030 and 2050 for each station by averaging the 50 projections for each day, then calculated the mean daily temperature by averaging the minimum and maximum temperatures on each day, and then averaged the daily mean temperature and precipitation across the 88 stations to produce average regional daily weather projections for the Central Queensland area. We used the same approach to derive baseline daily values for Central Queensland based on data measured at each weather station on each day during 2004–2013, which were provided by BOM (BOM, written communication, 2014).

A limitation of averaging the rainfall over all 88 stations in the region was that if rainfall was projected for any station on any day, the rainfall value for that day in the averaged series would not be zero. Consequently, some rainfall was projected for nearly every day in 2030 and 2050, potentially overstating the effect of climate change on salmonellosis as a consequence of increased rainfall.

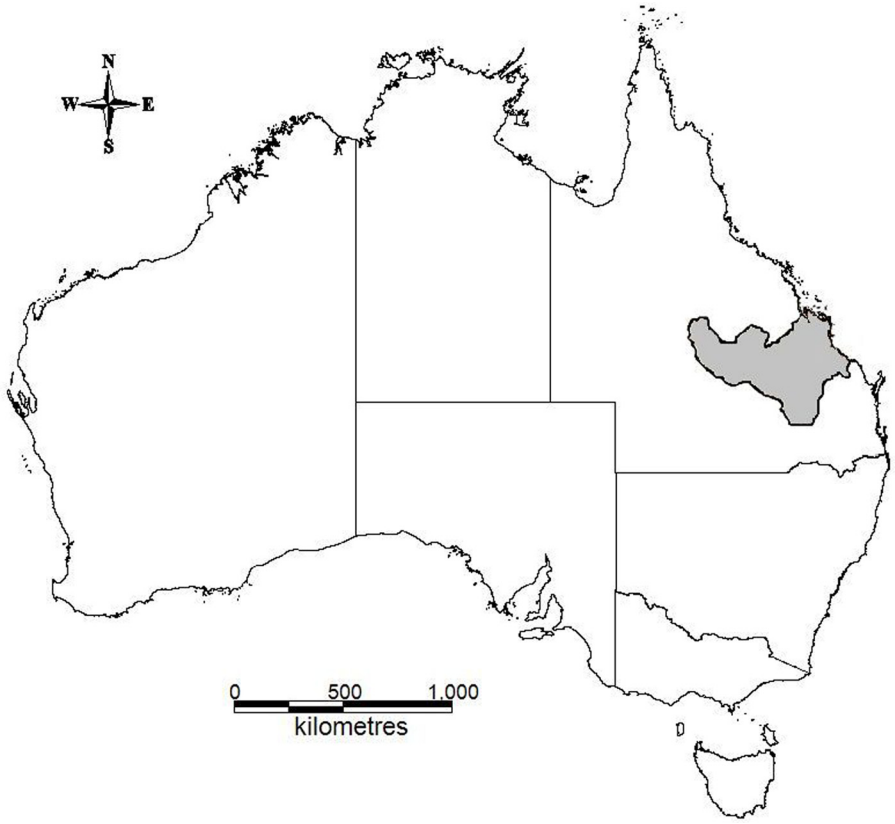

Figure 2. The location of Central Queensland in Australia.

Transition Probabilities

We required the following age- and sex-specific probabilities: *a*) contracting salmonellosis in baseline and climate change scenarios, *b*) being hospitalized for severe salmonellosis or developing PI-IBS or ReA following salmonellosis, *c*) fertility, mortality, and emigration.

We calculated the baseline probability of contracting salmonellosis by 5-y age group and sex from the daily number of salmonellosis cases in Central Queensland reported to Queensland Health between 1 January 2004 and 31 December 2013. Salmonellosis is a legally notifiable disease in Queensland; however, reported cases under-represent community incidence because some affected individuals do not seek medical care, and some cases are not tested for *Salmonella* or may have a false negative test result (Hall et al. 2008). To account for under-reporting, we multiplied the number of reported cases by age group and sex by 7, as recommended by Hall et al. (2008) according to their estimate of the proportion of salmonellosis cases likely to be under-reported in Australia during 2001–2005; this estimate was based on survey information regarding the probability that an individual with gastrointestinal symptoms would visit a doctor and have a stool test, the probability of a false negative or false positive stool test, and the probability that a positive case would be appropriately reported. To limit our analysis to the number of cases most likely to be influenced by climate change within Queensland, we reduced the estimated number of cases for each age group and sex to account for salmonellosis infections that were not foodborne (28%) and those not acquired in Australia (15%) using estimated proportions reported by the Australian Department of Health for 2010 based on a review of information from multiple sources (Kirk et al. 2014). The estimated case numbers were divided by the average population by age group and sex during 2004–2013 (ABS 2014) to estimate the baseline incidence rate of salmonellosis by age group and sex. The average annual incidence rates between 2004 and 2013 by age group and sex are presented in Table 2.

From the literature, we obtained the age- and sex-specific probabilities of transitioning from salmonellosis to ReA or PI-IBS or of being hospitalized for severe salmonellosis and the probability of dying or returning to health from these states (see Table 2). Batz et al. (2014) estimated that 1.9% of cases of salmonellosis required hospitalization, from which 0.04% of individuals died and 99.96% recovered. We could not identify reliable data for the age- or sex-specific proportions of hospitalized salmonellosis cases or cases that resulted in death, although we acknowledge that these differences likely exist, and as such, these figures from Batz et al. (2014) were applied for all ages and across both sexes.

Authors of an exhaustive literature review to estimate the incidence of salmonellosis and its sequelae in Australia circa 2010 concluded that approximately 8.5% of individuals with salmonellosis subsequently developed ReA (Ford et al. 2014). ReA appears to affect women and adults more than men and children. For example, a Dutch case–control study of 193 cases of salmonellosis found that 88% of ReA cases resulting from salmonellosis occurred in women, and all cases occurred in individuals >23 y of age, although this information was drawn from 8 ReA cases (Doorduyn et al. 2008). In a larger sample of 261 individuals affected by a salmonellosis outbreak in South Australia in 1999, 12% of 207 children affected developed ReA within the following 6–12 mo, as did 24% of the 54 adults surveyed (Lee et al. 2005). Similarly, of 204 individuals with rheumatological symptoms interviewed within 8 wk of a culture-confirmed case of salmonellosis between 2002 and 2004 in two U.S. states, 14% of cases occurred in individuals ≤18 y of age (Townes et al. 2008). Although only 4% of cases were confirmed as ReA, these studies

Table 2. Input parameters for variables in the microsimulation models, which varied by age and sex.

Age (y) and sex	Baseline salmonellosis cases per 1,000 population[b]	Percentage of transitions between salmonellosis and other health states[a]				Emigration[d,e]
		Healthy[c]	Hospital[c]	PI-IBS[c]	ReA[c]	
Females						
0–9	13.9	77.1	1.9	9.4	11.7	0.0084
10–19	1.6	76.9	1.9	9.6	11.7	0.0331
20–29	2.1	45.5	1.9	36.0	16.6	0.0229
30–39	1.4	57.0	1.9	24.5	16.6	0.0184
40–49	1.9	68.5	1.9	13.0	16.6	0.0280
50–59	2.3	68.5	1.9	13.0	16.6	0.0670
60–69	2.8	77.7	1.9	3.8	16.6	0.0045
≥70	3.8	77.7	1.9	3.8	16.6	0.0000
All ages	3.9	69.5	1.9	13.6	15.0	NA
Males						
0–9	15.0	92.1	1.9	4.4	1.6	0.0348
10–19	2.0	92.0	1.9	4.5	1.6	0.0097
20–29	2.3	78.9	1.9	16.9	2.3	0.0327
30–39	1.5	84.3	1.9	11.5	2.3	0.0008
40–49	1.6	89.7	1.9	6.1	2.3	0.0450
50–59	2.1	89.7	1.9	6.1	2.3	0.0281
60–69	2.4	94.0	1.9	1.8	2.3	0.0250
≥70	2.3	94.0	1.9	1.8	2.3	0.0240
All ages	3.9	89.7	1.9	6.4	2.0	NA

Note: Transitions between salmonellosis and death were set to occur in 0.04% of cases for all age groups and both sexes; however, this resulted in no deaths in either the baseline or the climate change scenario. For incidence rates of salmonellosis under climate change, which varied by age, sex, and year between 2016 and 2036 based on the projected weather and weather–salmonellosis association derived through the method described in "Methods," see Appendix L of Stephen (2017). NA, not applicable; PI-IBS, post-infectious irritable bowel syndrome; ReA, reactive arthritis.

[a]The percentage of transitions between salmonellosis and other health states applies to both the baseline and climate change scenarios.

[b]Baseline cases of salmonellosis are the average annual incidence of salmonellosis between 2004 and 2013 based on the annual adjusted reported cases of salmonellosis during 2004–2013 (Queensland Health, written communication, 2015) divided by the annual population as of 30 June of each year between 2004 and 2013 (ABS 2014), and averaged over the 10-y period and multiplied by 1,000.

[c]The proportion of cases by age and sex that were hospitalized is from Batz et al (2014); the proportion of cases by age and sex that developed PI-IBS is from Thabane et al. (2007), Neal et al. (1997), and Thabane and Marshall (2009); and the proportion of cases by age and sex that developed ReA is from Doorduyn et al. (2008), Lee et al. (2005), and Townes et al. (2008). The proportion of cases that returned to healthy after salmonellosis is those who were not hospitalized and did not develop PI-IBS or ReA.

[d]The figures for emigration are transition probabilities.

[e]Emigration transition probabilities were calculated and applied in the simulation by age and sex; as such, no emigration probabilities were calculated for all ages.

indicate that ReA can occur in children, but at a lower incidence than in adults. For the present study, we adopted the figure of 88% of cases occurring in females, and we allocated approximately 13% of cases to individuals 0–19 y of age (age groups were 10-y blocks, so this figure could not be applied to those 0–18 y of age).

A systematic review of 18 studies in 8 countries found a pooled incidence rate for PI-IBS of 10% following gastrointestinal infections (Thabane et al 2007). Other studies have made similar estimates of 8.5% (Haagsma et al. 2010) and 7% (Neal et al. 1997), although estimates vary from 4–35% (Ford et al. 2014; Thabane and Marshall 2009). We selected the 10% incidence rate for the current study because Thabane et al. (2007) examined the largest number of studies, and those studies were predominantly set in countries such as the United Kingdom and Canada, which have similar sociodemographic characteristics and health systems to Australia's. Thabane et al. (2007) and Thabane and Marshall (2009) reported that younger individuals were more likely to develop PI-IBS, which has been supported by Neal et al. (1997), who found that six months after a bacterial infection, 34% of 19–29-y-olds experienced altered bowel habits compared with 26% of 30–44-y-olds, 31% of 45–59-y-olds, and 9% of individuals >60 y old. We adopted these age-specific proportions for the present study, and women were allocated 68% of cases because women are also reported to be between 1.5 and 3.4 times more likely than men to develop PI-IBS (Neal et al. 1997; Thabane and Marshall 2009). Neither PI-IBS nor ReA is life-threatening; therefore, all individuals with these conditions returned to healthy.

The overall probabilities for transitions between states are shown next to each transition pathway in Figure 1 for demonstrative purposes, and the age- and sex-specific proportions of cases that required hospitalization, developed PI-IBS or ReA, or returned to healthy are shown in Table 2. The microsimulation model uses annual rates; thus, the probabilities were transformed to rates using $-\log_e(1-p)/\Delta t$ where Δt was 1 y.

We initially ran the models from 2008–2036, and the early results clearly showed that the base population required a period of time, or burn-in, for the model to begin transitioning individuals at the expected rates. Because all individuals started the simulation as susceptible to salmonellosis, that is to say, in the "healthy" state, elevated annual rates of salmonellosis and reduced rates of sequelae conditions were initially observed. This phase occurred in the simulated period from 2008 to 2015, and this period of time was excluded as a burn-in. Model simulations for 2016–2036 were used as results. The model allowed individuals to be in only one health state at once; as such, only individuals who were in the "healthy" state were susceptible to salmonellosis, and all individuals in other health states, such as PI-IBS or ReA, were immune to a new infection until the duration of that state had passed.

Weather–Salmonellosis Associations

To determine the probability of contracting salmonellosis under climate change, we calculated the associations between salmonellosis incidence and mean temperature and rainfall using 2004–2013 as the baseline period. Figure 3 shows the average monthly cases of salmonellosis, mean temperature (degrees Celsius), and rainfall (millimeters) between 2004 and 2013.

Weather data. We acquired recordings of daily minimum and maximum temperatures and rainfall from weather stations in Central Queensland for 1 January 2004 to 31 December 2013 from BOM (BOM, written communication, 2014). We included 10 temperature stations with <6% missing data and 46 rainfall stations with no missing data. We imputed missing temperature data using RClimTool (Herrera 2014). We calculated regional

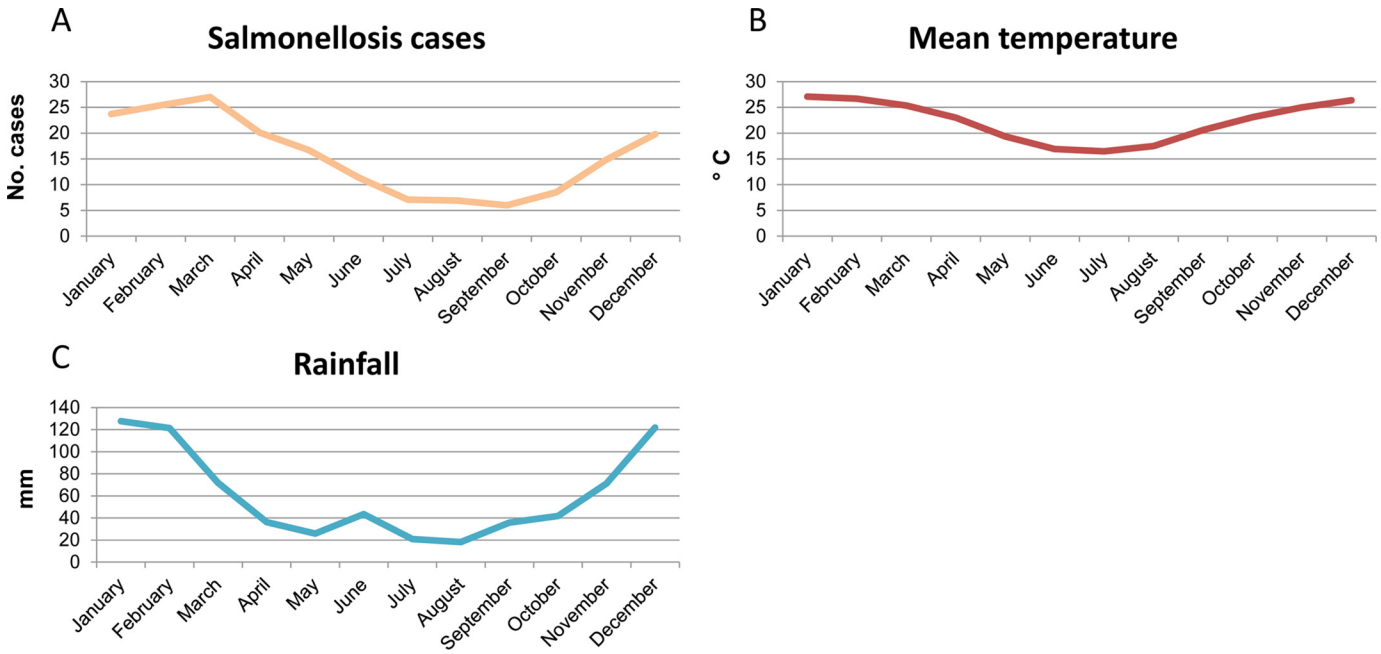

Figure 3. Average monthly number of (*A*) salmonellosis cases, (*B*) mean temperature, and (*C*) rainfall in Central Queensland between 2004 and 2013. Salmonellosis cases were sourced from Queensland Health's Communicable Disease database (Queensland Health, written communication, 2015), adjusted for under-reporting, nonfoodborne cases, and cases not acquired locally, and averaged for each month. Weather data were sourced from the Australian Bureau of Meteorology (BOM, personal communication, 2014) for individual weather stations in Central Queensland. We calculated the mean regional temperature and rainfall by averaging the daily data from the individual stations and then calculated the mean monthly temperature and rainfall for the region over the 2004–2013 period by averaging the daily data over the months.

daily rainfall and minimum, mean, and maximum temperatures by averaging recordings across all stations.

Disease notification data. We obtained the daily number of salmonellosis cases reported in Central Queensland from 1 January 2004 to 31 December 2013 from Queensland Health (J. Marquess, Queensland Health, personal communication). The date of the case was the date a patient's stool sample was collected, which is the closest available date to when infection occurred. Queensland Health introduced a more sensitive test for salmonellosis in August 2013, which likely affected the number of notifications recorded thereafter (R. Stafford, epidemiologist, Queensland Health, personal communication, 30 April 2015). We adjusted for this step-change in our models described below.

Analysis. We fitted a Poisson regression model for daily salmonellosis cases with distributed lags of 21 d for daily mean temperature and rainfall using natural splines with 3 degrees of freedom and a lag −1 autoregressive term as predictors. We used a lag of 21 d because this was a plausible time frame in which *Salmonella* could be transmitted to humans through food chains involving animal products or produce. We controlled for upward trends in cases over time caused by increasing population and other factors unrelated to weather by including quadratic and linear terms for time. We also identified that notifications were influenced by day of the week and public holidays; therefore, we modeled these using categorical variables and added a binary variable for days after 1 August 2013 to account for the new pathology test. The model was as follows:

$$s_t \sim \text{Poisson}(\mu_t)$$

$$\log_e(\mu_t) = \rho s_{t-1} + \alpha X_t + \beta \text{temperature}_t + \gamma \text{rainfall}_t,$$

where s_t is the number of cases on day t, and $\mathbf{X}$ is a design matrix that fits the intercept, day of the week, public holiday, trend, and change in pathology test.

This model estimated that salmonellosis incidence increased by 87.1% (95% credible interval (Cr) 72.0%, 103.6%) following a day with a mean temperature of 28°C (the 95th percentile temperature) compared with a 23°C day, the 50th percentile temperature. Cases also increased by 22.3% (95% CrI: 0.3%, 49.1%) after 12 mm of rainfall, also the 95th percentile, compared with a day with 2 mm of rainfall, the 80th percentile. See Stephen and Barnett (2016) for further details of this method. To translate these associations into the salmonellosis risk under climate change, we calculated the risk of salmonellosis for every possible combination of temperature and rainfall in 0.5°C and 1-mm increments, respectively, that occurred during the 2004–2013 baseline period. To ensure we could match these risks to possible temperature–rainfall combinations that occurred in the projected data but not during the 2004–2013 period, we used inverse distance weighting to generate estimates of the salmonellosis risk for temperature–rainfall combinations surrounding the existing combinations (Isaaks and Srivastava 1989). We then matched this set of risks at possible temperature–rainfall combinations to the projected temperature–rainfall combination for each day in 2030 and 2050, giving the daily relative risk of salmonellosis in 2030 and 2050.

We summed the daily relative risks in 2030 and 2050 and divided them by the summed daily relative risks for the baseline period to produce a relative risk ratio (RRR) of salmonellosis under climate change in 2030 and 2050 compared with the baseline period. From these data, we linearly interpolated the risks for the years 2008–2029 and 2031–2036, assuming that the risks changed at a constant annual rate over the time period.

We derived age- and sex-specific rates of salmonellosis by multiplying the total RRR by the proportions of cases according to age group and sex, and we converted the resulting age- and sex-specific risk estimates to instantaneous rates for use in the microsimulation model. This approach differs from the more commonly used approach for calculating rates, in which the

dynamic at-risk population is included in the Poisson regression models as an offset [for example, see Alho and Spencer (2005)]. Therefore, we compared the transition rates derived using both methods to assess the potential impact of the alternative method on our estimates.

Health and Economic Costs

Based on Batz et al (2014), the probability of mortality among individuals with severe salmonellosis in our model was 0.004% of hospitalized cases; therefore, it was consistent with expectations that there were no deaths caused by salmonellosis in the simulated population. Consequently, our estimates of costs due to years of health lost, the economic value of these lost years, and medical expenditures are limited to costs associated with morbidity due to salmonellosis or the sequelae conditions.

We have calculated three costs: the health costs, the morbidity costs, and the economic costs of salmonellosis and its sequelae. The health costs refer to the number of quality-adjusted life years (QALYs) lost, which was calculated by multiplying the number of days that simulated individuals spent in each unwell state (salmonellosis, hospitalized, recovering from severe salmonellosis, ill with ReA, or ill with PI-IBS) by the corresponding disability weight for that state (Figure 1) and summing the resulting values for the population as a whole. We then calculated the morbidity costs as the economic value of the years of healthy life lost by multiplying the QALYs for each outcome by AUD64,000, the average amount that Australians surveyed by Shiroiwa et al. (2010) indicated they were willing to pay to gain a year of full health. We incorporated the uncertainty of this estimate by sampling from a normal distribution with a mean of AUD64,000 and a standard deviation of AUD2,041 (based on the 95% confidence interval of AUD60,000–AUD68,000) (Shiroiwa et al. 2010).

We searched the literature for papers that described the typical health care usage for the health states in our model. We could not find an appropriate paper for ReA; hence, the health care costs for this condition were not included. Typical health care usages were then combined with Australian cost data from the Medicare Benefits Schedule (RACGP 2014) and National Hospital Cost Data Collection (IHPA 2013). For example, a hospitalization for severe salmonellosis was matched with the hospital admission code "gastroenteritis with catastrophic or severe complications," which had a total cost of AUD6,872, which includes bed days, tests, and clinicians' time. These health care costs were added to the morbidity costs, and we refer to this value as the economic cost of salmonellosis and its sequelae.

Costs incurred in the future are typically valued less than those incurred at present because present costs defer resources from being immediately invested elsewhere, thus disallowing a positive return on such investments (Drummond et al. 2015). Individuals also tend to value benefits received immediately more than those received in the future (Mathers et al. 1999). To reflect this valuation, we applied annual discounting of 3% to both the health and economic costs to reduce future costs for each year in the future they occur. A 3% discount aligns this study with key studies of disease costs such as the earlier Australian and Global Burden of Disease (BOD) studies (Mathers et al. 1999; Begg et al. 2007; WHO 2008), although discounting has since been removed from the later BOD studies (Australian Institute of Health and Welfare 2016). Discounting was applied by multiplying the annual health costs and the annual economic costs by the discount factor derived using the following formula: $Dn = 1/(1+r)^n$, where Dn is the discount factor, r is the 3% discount rate, and n is the number of years in the future starting from 2016. We then summed the discounted annual costs to calculate the total discounted health and economic costs between 2016 and 2036. We present both the discounted and undiscounted results.

We used two different approaches to compare the results of the microsimulation models with expectations. First, we compared the age- and sex-specific percentages of transitions from salmonellosis to health or to a sequelae condition obtained from the simulation with expectations based on the literature. Second, we compared the simulated population structure for 2036 with age- and sex-specific population projections for Central Queensland in 2036 from the QGSO (2014).

Results

The baseline population had 199,539 individuals [based on the estimated count on 30 June 2007 from the ABS (2008)] and was projected by the QGSO (2014) to be 355,409 in 2036. Age- and sex-specific percentages of transitions from salmonellosis to health or to a sequelae condition in the simulated population were consistent with expectations for the literature-based transition rates used as model inputs (see Table S2). For example, 4.3% of simulated males 0–9 y old transitioned from salmonellosis to PI-IBS, consistent with the 4.4% transition rate used in our model. In addition, the distribution of the simulated Central Queensland population with regard to age and sex was generally consistent with QGSO projections for 2036 (see Figure S1).

Averaging the weather projections data somewhat tempered projections of extremes; however, substantial variation in weather was still observed in the data. For example, mean daily temperatures ranged between 15.3°C and 28.9°C. Central Queensland was projected to experience a 1.8% increase in annual mean temperature and a 3.5% decrease in annual rainfall by 2036 under the A1FI scenario.

We compared the rates of transitioning to salmonellosis under mean temperature and rainfall between 2004 and 2013 calculated using a method that incorporated the at-risk population structure as a final step at the end of the calculations with rates calculated using the more standard approach of incorporating the at-risk population in the regression models, as described by Alho and Spencer (2005), and found minimal differences in the rates (see Figure S2), indicating that the rates were acceptable.

The RRR of salmonellosis under climate change in 2036 was 1.11 compared with the 2004–2013 baseline period. This RRR represents the relative difference between the summed daily RRs for salmonellosis for the daily temperature and rainfall combinations observed in 2004–2013 and the summed daily RRs for salmonellosis for the daily temperature and rainfall combinations projected under climate change in 2036.

In the baseline scenario with no change in climate, we estimated that the population of Central Queensland would lose 456.0 QALYs (95% CI: 440.3, 473.1) to salmonellosis and its sequelae between 2016 and 2036, at a total cost (lost QALYs plus direct medical expenditures) of AUD29,900,000 (95% CI: AUD28,900,000, AUD31,100,000) (Table 3). Under climate change, we estimated that 485.9 QALYs would be lost (95% CI: 469.6, 503.5) at a total cost of AUD31,900,000 (95% CI: AUD30,800,000, AUD33,000,000).

When discounting was applied, the total cost between 2016 and 2036 was 339.2 QALYs (95% CI: 328.1, 352.8) and AUD22,300,000 (95% CI: AUD21,500,000, AUD23,200,000) in the baseline scenario and 358.6 QALYs (95% CI: 346.7, 372.5) and AUD23,500,000 (95% CI: AUD22,700,000, AUD24,400,000) under climate change. The discounted and undiscounted costs for the individual health states are presented in Table 3.

Under climate change, we estimated that 20,400 cases of acute salmonellosis would occur between 2016 and 2036 (95%

Table 3. Estimated health and economic costs of salmonellosis and its sequelae during 2016–2036 in the baseline and climate change scenarios with 95% confidence intervals.

	Baseline scenario without climate change			Climate change scenario[a]		
State	Cases	QALYs lost	Total cost (Australian dollars)[b,c]	Cases	QALYs lost	Total cost (Australian dollars)[b,c]
Undiscounted costs						
Salmonellosis	18,387 (18,182, 18,557)	34.7 (34.3, 35.0)	2,200,000 (2,200,000, 2,200,000)	20,014 (19,714, 20,274)	37.8 (37.2, 38.3)	2,400,000 (2,400,000, 2,500,000)
Hospitalized[d]	344 (314, 378)	3.2 (2.9, 3.5)	720,000 (680,000, 770,000)	385 (352, 412)	3.6 (3.3, 3.8)	750,000 (720,000, 790,000)
ReA	1,413 (1,362, 1,464)	112.0 (108.0, 116.1)	7,200,000 (6,900,000, 7,400,000)	1,550 (1,488, 1,608)	122.9 (118.0, 127.5)	7,900,000 (7,600,000, 8,200,000)
PI-IBS	1,457 (1,405, 1,517)	306.1 (295.1, 318.5)	19,800,000 (19,100,000, 20,600,000)	1,532 (1,481, 1,590)	321.7 (311.1, 333.9)	20,800,000 (20,200,000, 21,600,000)
Total	21,602 (21,263, 21,915)	456.0 (440.3, 473.1)	29,900,000 (28,900,000, 31,100,000)	23,482 (23,036, 23,884)	485.9 (469.9, 503.5)	31,900,000 (30,800,000, 33,000,000)
Discounted costs						
Salmonellosis	18,387 (18,182, 18,557)	25.8 (25.5, 26.1)	1,700,000 (1,600,000, 1,700,000)	20,014 (19,714, 20,274)	28.0 (27.6, 28.4)	1,800,000 (1,800,000, 1,800,000)
Hospitalized[d]	344 (314, 378)	2.4 (2.2, 2.6)	540,000 (500,000, 570,000)	385 (352, 412)	2.7 (2.4, 2.8)	560,000 (530,000, 590,000)
ReA	1,413 (1,362, 1,464)	83.0 (79.8, 85.9)	5,300,000 (5,100,000, 5,500,000)	1,550 (1,488, 1,608)	90.8 (87.2, 94.4)	5,800,000 (5,600,000, 6,000,000)
PI-IBS	1,457 (1,405, 1,517)	228.0 (220.6, 238.2)	14,800,000 (14,300,000, 15,400,000)	1,532 (1,481, 1,590)	237.2 (229.5, 247.0)	15,400,000 (14,900,000, 16,000,000)
Total	21,602 (21,263, 21,915)	339.2 (328.1, 352.8)	22,300,000 (21,500,000, 23,200,000)	23,482 (23,036, 23,884)	358.6 (346.7, 372.5)	23,500,000 (22,700,000, 24,400,000)

Note: The set of parameters used to derive these estimates is provided in Table 1. Costs are totals for the 2016–2036 period. PI-IBS, post-infectious irritable bowel syndrome; QALYs, quality-adjusted life years; ReA, reactive arthritis.
[a]The parameters used for the climate scenarios differ primarily on the incidence rate of salmonellosis under baseline weather or projected mean temperature and rainfall between 2016 and 2036, which is increased under climate change. The A1FI climate change scenario assumes very rapid economic growth and technological change, population growth that peaks mid-21st century, and a continued reliance on fossil fuels (IPCC 2000).
[b]Total cost represents the willingness-to-pay value applied to the QALYs lost to each condition, plus direct medical expenditures for salmonellosis, hospitalization, and PI-IBS only.
[c]The confidence intervals for total cost are the 95% confidence intervals for the monetary cost if Australians paid AUD60,000 or AUD68,000 to gain one year of perfect health.
[d]The estimated costs for hospitalizations include a 3-d posthospital recovery period.

CI: 20,066, 20,685), compared with 18,731 (95% CI: 18,496, 18,934) under the baseline scenario (Table 3). Total costs of acute cases accounted for a small proportion of the total costs under either scenario (approximately 8%) because of the relatively small number of lost QALYs [$(4\text{ d}/365)\times 0.197 = 0.00216$ QALYs $\times$ AUD64,000 = AUD138/case 0021, plus AUD42.90 each for the 20% of cases who sought medical attention (Hall et al. 2008) as the direct medical expenditures]. The majority of estimated costs (approximately two-thirds) were associated with PI-IBS, primarily due to lost QALYs (estimated direct medical expenses per case of PI-IBS = AUD1,396; costs of lost QALYs/case = 5-y duration $\times$ 0.042 $\times$ AUD64,000 = AUD13,440). Based on the value of lost QALYs only (because we did not account for direct medical expenditures), ReA accounted for approximately 25% of total costs (AUD5,077/case). Hospitalization due to severe salmonellosis was estimated at direct medical expenditures of AUD6,872 per case (72% of the total cost) plus AUD592 per hospitalization for lost QALYs [$(6\text{ d}/365)\times 0.563 = 0.00925$ QALYs $\times$ AUD64,000 0092 and an additional AUD74 for lost QALYs during a 3-d recovery period.

The proportions of estimated costs of salmonellosis accounted for by sex and age groups were similar for the baseline and climate change scenarios because climate change did not influence these characteristics, and differences between the simulated populations were therefore due to random variation only (data not shown). The estimated costs of salmonellosis and its sequelae for females were approximately twice the estimated costs for males, with females incurring 66.3% of the total costs owing to their increased rate of sequelae conditions (Table 4). Estimated costs were highest for younger age groups (Table 5) owing to the higher incidence of acute salmonellosis in this group (Table 2), with children 0–9 y old accounting for 34% of the total costs. Individuals 30–39 y old and 20–29 y old had the next highest estimated costs, consistent with the relatively high rate of PI-IBS in these age groups (Table 2) (Thabane et al 2007).

Discussion

Estimates from our microsimulation analysis suggest that the risks of salmonellosis and its sequelae, and the resulting health and economic costs, will increase in Central Queensland under the influence of climate change until 2036. Our model assumed higher risks of salmonellosis and its sequelae in females than in males, and in younger children than in other age groups, consistent with the literature; therefore, the higher estimated costs for these groups (for both the climate change and baseline climate scenarios) were consistent with expectations. PI-IBS accounted for the majority of the estimated costs, regardless of assumptions about climate change, because of its 5-y duration and the resulting loss of QALYs. We found that microsimulation models were a useful technique for modeling the influence of climate change on disease processes. With microsimulation, we were able to integrate several complicated associations—weather, salmonellosis incidence, time, and demographic influences—to produce clear estimates of the health and economic costs of salmonellosis (and capture projection uncertainty) and to identify the primary drivers of these costs. Higher incidence rates of salmonellosis assumed for children, of PI-IBS for young adults, and of sequelae conditions for females were key drivers of the estimated costs of salmonellosis in Central Queensland under climate change and baseline scenarios. Policy makers and local authorities may be able to use this information in developing preventative strategies targeted for these groups. For example, educating parents, child care workers and early-education teachers about food hygiene practices could reduce salmonellosis cases and costs for young

Table 4. Percentage and 95% confidence intervals of the estimated costs by sex, and the proportion of the costs accounted for by each health state in the baseline scenario without climate change.

State	Percentage of costs by sex		Percentage of costs by health state	
	Males	Females	Males	Females
Salmonellosis	51.8 (41.6, 62.7)	48.2 (38.2, 59.0)	11.0 (8.8, 13.3)	5.2 (4.1, 6.4)
Hospitalized[a]	51.1 (32.9, 95.9)	48.9 (32.2, 93.0)	1.7 (1.1, 3.2)	0.8 (0.5, 1.6)
ReA	19.7 (12.8, 37.8)	80.3 (40.1, 132.9)	14.6 (9.5, 28.1)	30.4 (15.1, 50.2)
PI-IBS	36.7 (16.7, 68.6)	63.3 (29.2, 108.4)	72.6 (33.0, 135.6)	63.6 (29.4, 109.0)
Total	33.7 (17.7, 60.7)	66.3 (32.6, 110.8)	100.0	100.0

Note: Estimated cost represents the willingness-to-pay value applied to the quality-adjusted life years (QALYs) lost to each condition, plus direct medical expenditures for salmonellosis, hospitalization, and PI-IBS only. The set of parameters used to derive these estimates is provided in Table 1. PI-IBS, post-infectious irritable bowel syndrome; ReA, reactive arthritis.
[a]The estimated costs for hospitalizations include a 3-day post-hospital recovery period.

children. Broader media campaigns geared toward children and their parents raising awareness about food safety information and of the prevalence and potential sequelae of salmonellosis may also serve to reduce cases and costs of salmonellosis.

Food Standards Australia New Zealand (FSANZ) estimated that it would cost the Australian broiler industry AUD11,000,000 in the first year and AUD4,000,000 each year thereafter to introduce regulations for foodborne pathogen contamination (FSANZ 2010). This is a substantially lower cost than those absorbed by the community through foodborne disease, estimated by FSANZ to be AUD14,000,000 to AUD74,000,000 annually (FSANZ 2010). Regulation could be a cost-effective means to reduce foodborne disease incidence in Australia, particularly because, as we found in this study, the costs are likely to increase in the future under climate change. Microsimulation models could also be used to estimate the cost savings in Australia of interventions to reduce the incidence of foodborne diseases.

The primary strength of this study is that, to our knowledge, we are the first to report estimates of the costs of salmonellosis in Queensland and to evaluate the factors that may be driving these costs. This information may be used to inform health policies. We also believe that this is the first study to estimate the health and economic costs of a disease related to climate change using microsimulation. We demonstrated that microsimulation is a useful tool for modeling complex interactions between weather, disease, and demographic variables, and it can provide a wealth of data. Some examples of how these rich data could be used include plotting the projected rates of salmonellosis over time by age group and sex, examining the projected cases in school-age children to estimate days lost from school, and examining the projected numbers of severe sequelae in the elderly to plan future hospital demand. We plan to share the data from our microsimulation models to allow other researchers and policy makers to combine or isolate data of interest to them.

One limitation of this study is the assumptions made in the microsimulation models. We assumed that between 2016 and 2036, there would be no changes in *a*) the association between weather and salmonellosis and *b*) the susceptibility of humans to salmonellosis or to climate change through changes in infrastructure, improved information about behaviors to avoid contracting salmonellosis, or individuals' social or economic circumstances. Such adaptations can be built into microsimulation models by adjusting the relative risks of the weather–disease associations (Gosling et al. 2017).

Another limitation is the uncertainty in the cost estimates generated. We confirmed that model projections were consistent with expectations given our assumptions (model inputs) regarding changes in the population over time [by comparing our simulated population with projections by the QGSO (2014)] and the age- and sex-specific probabilities of developing a sequelae condition (by comparing incidence rates in the simulation population with the rates used as model inputs). We also took the average of 100 simulations and calculated confidence intervals to quantify the uncertainty introduced by stochastic decisions within the models. However, we were unable to control for or quantify other sources of uncertainty in the parameters, such as uncertainty in the effects of weather on salmonellosis or uncertainty in the extent of underreporting of salmonellosis cases.

Our microsimulation also assumed that the duration of each state was fixed and constant for all individuals. We selected values for the duration of each state from the literature, using the average or most likely value when known (Table 1). If the values used reflect true durations, and if the range of possible durations is normally distributed and constant among population subgroups, then the durations used should produce population-level estimates that are correct on average. However, future studies should investigate methods to sample durations for each incident case from a range of possible values to more accurately estimate the time that simulated individuals were in each health state.

We have likely overestimated the costs of hospitalizations and sequelae conditions. Salmonellosis cases that are reported to health departments are typically more severe than cases that are not reported. In adjusting the number of reported cases of salmonellosis to account for under-reporting, we "added" the low-severity cases that were not reported. However, the probabilities of hospitalization and of developing sequelae conditions were drawn from studies of the outcomes of reported cases of salmonellosis. In applying these figures to the adjusted number of salmonellosis cases, we transitioned too many mild cases to hospitalizations and sequelae conditions, although the extent of this overestimation cannot be quantified. In addition, we were unable to identify suitable data to enable us to estimate the medical expenditure costs, and therefore the total economic costs, for ReA.

Further, we examined only one climate change scenario, based on the A1FI emissions scenario (which assumes that emission levels will continue at current levels) and composite projections from 6 global climate models that have been proposed for the Queensland area (BOM, written communication, 2014). Although we believe that this scenario is a reasonable choice, future studies should consider multiple scenarios to better capture uncertainty regarding the future effects of climate change.

We also note that we used a method to calculate the transition rate to salmonellosis under weather conditions that incorporated the at-risk population structure in a final series of calculations at the end of the process, instead of the standard approach, which includes the at-risk population in the regression models. Although we found that our method produced very similar results to the standard method, we recommend that the standard method be used in future studies.

As noted above, we identified that the model needed a period of years to burn-in before performing as expected. To reduce the length of the burn-in phase, we recommend that where possible,

Table 5. Percentage and 95% confidence intervals of the estimated costs by age group, and the proportion of the costs accounted for by each health state in the baseline scenario without climate change.

Health state	Age group (y)									Total
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	≥80	
Percentage by age for each health state										
Salmonellosis	49.0 (42.9, 55.0)	6.1 (4.2, 8.1)	7.3 (5.3, 9.5)	5.1 (3.4, 7.0)	6.2 (4.4, 8.1)	6.9 (5.2, 8.8)	7.8 (6.1, 9.8)	6.7 (5.0, 8.7)	4.9 (3.4, 6.7)	100.0 (79.8, 121.0)
Hospitalizeda	30.6 (8.4, 59.2)	8.9 (7.1, 17.6)	9.4 (7.1, 19.1)	8.6 (7.1, 15.8)	8.6 (7.1, 16.0)	8.7 (7.1, 16.0)	8.6 (7.1, 16)	8.4 (7.1, 15.3)	8.2 (7.1, 13.9)	100.0 (65.1, 188.9)
ReA	36.8 (21.4, 55.0)	5.5 (2.9, 10.7)	7.6 (3.0, 14.8)	7.0 (3.0, 13.8)	8.2 (4.1, 14.8)	8.0 (4.4, 14.1)	9.3 (5.1, 15.9)	9.5 (5.0, 16.2)	8.1 (4.0, 15.3)	100.0 (52.9, 170.7)
PI-IBS	31.6 (16.0, 49.1)	8.0 (3.0, 16.0)	13.6 (5.2, 24.4)	15.9 (6.3, 27.8)	8.7 (3.6, 16.9)	8.5 (3.6, 15.8)	5.5 (2.7, 11.0)	4.0 (2.7, 8.0)	4.1 (2.7, 8.0)	100.0 (45.9, 177)
Total	34.1 (19.2, 51.1)	7.2 (3.1, 14.1)	11.6 (4.7, 20.9)	12.8 (5.3, 22.7)	8.4 (3.8, 15.7)	8.3 (4.0, 14.9)	6.7 (3.6, 12.2)	5.6 (3.5, 10.2)	5.2 (3.1, 9.8)	100.0 (50.3, 171.6)
Percentage of costs by health state										
Salmonellosis	10.3 (9.0, 11.5)	6.0 (4.1, 8.0)	4.5 (3.2, 5.9)	2.8 (1.9, 3.9)	5.3 (3.8, 7.0)	5.9 (4.5, 7.6)	8.4 (6.5, 10.5)	8.6 (6.4, 11.1)	6.7 (4.6, 9.1)	7.2 (5.7, 8.7)
Hospitalized[a]	1.0 (0.3, 2.0)	1.4 (1.1, 2.8)	0.9 (0.7, 1.9)	0.8 (0.6, 1.4)	1.2 (1.0, 2.2)	1.2 (1.0, 2.2)	1.4 (1.2, 2.7)	1.7 (1.4, 3.1)	1.8 (1.5, 3.0)	1.1 (0.7, 2.1)
ReA	27.0 (15.7, 40.4)	18.9 (9.9, 36.9)	16.5 (6.5, 32.0)	13.7 (5.9, 27.0)	24.4 (12.1, 44.4)	24.3 (13.4, 42.7)	34.8 (19.0, 59.5)	42.2 (22.3, 72.3)	39.1 (19.1, 73.3)	25.1 (13.3, 42.8)
PI-IBS	61.7 (31.3, 96.0)	73.7 (27.8, 147.0)	78.1 (29.7, 140.4)	82.7 (32.9, 144.4)	69.1 (28.6, 134.3)	68.6 (28.9, 127.3)	55.4 (27.2, 109.6)	47.6 (32.3, 94.2)	52.4 (34.9, 102.1)	66.7 (30.6, 118)
Total	100.0 (56.3, 149.9)	100.0 (43, 194.6)	100.0 (40.2, 180.1)	100.0 (41.4, 176.6)	100.0 (45.5, 187.8)	100.0 (47.8, 179.8)	100.0 (53.9, 182.3)	100.0 (62.4, 180.6)	100.0 (60.2, 187.6)	100.0 (50.3, 171.6)

Note: Estimated cost represents the willingness-to-pay value applied to the quality-adjusted life years (QALYs) lost to each condition, plus direct medical expenditures for salmonellosis, hospitalization, and PI-IBS only. The set of parameters used to derive these estimates is provided in Table 1. PI-IBS, post-infectious irritable bowel syndrome; ReA, reactive arthritis.
[a]The estimated costs of hospitalizations include a 3-day post-hospital recovery period.

future studies begin their starting population with a representative distribution of the states or demographic factors to be modeled, such as in a state of ill health or with some women pregnant, to more quickly reach expected levels of illness, sequelae conditions, and population growth.

Conclusion

Results from our microsimulation model of salmonellosis through 2036 in Central Queensland suggest that health and economic costs are likely to be higher under the climate change scenario that we evaluated than under a scenario that assumes no changes in climate. Salmonellosis already incurs substantial costs to the community, making it worthy of preventative action to reduce the cost. The key cost drivers in both the baseline and climate change scenarios are the high rates of salmonellosis incidence in children and of sequelae conditions in females, particularly PI-IBS, which accounts for two-thirds of the total cost of salmonellosis. These drivers are based on input parameters that were sourced from the literature and are largely independent of climate change, except that the increased incidence of salmonellosis under climate change spurs the higher costs from both acute infections and sequelae. These findings highlight areas where preventions could be directed, such as local initiatives to improve the food hygiene practices of children, or broader measures such as introducing industry regulations to achieve reductions in salmonellosis and subsequent sequelae conditions throughout the population.

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